

### REMARKS/ARGUMENTS

The Office Action mailed August 28, 2002 and the Advisory Action mailed June 6, 2003 have been carefully reviewed and the foregoing amendments are made in response thereto. In view of the amendments and the following remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Applicants respectfully submit that no prohibited new matter has been introduced by the amendments. Claims 12 and 13 have been amended. Claims 10 and 11 have been canceled. Applicants reserve the right to pursue the cancelled Claims in a related application. Support for the amendments to claim 13 may be found on, e.g., page 4 of the specification (lines 17-21) and on page 10 (lines 7-16). Support for the amendments to claim 12 may be found on, e.g., page 5 of the specification (lines 1-2). Entry of the amendment is respectfully requested.

#### ***A. Objection to the Specification***

Claims 10-13 are objected to because Claim 13 includes a Markush group of names of "maintenance genes" that lacks proper punctuation. Applicants have amended Claim 13 to separate the gene/protein names by commas. Therefore, this objection to the specification is obviated.

#### ***B. Claim Rejections under 35 U.S.C. § 112***

Claims 10-13 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite, because Claim 13 does not indicate with what "said expression of said gene in said plurality of samples" is to be compared. Applicants have amended Claim 13 to clarify.

The Examiner further alleges that the language "using the expression of said at least three maintenance genes" does not apprise one of skill in the art as to how the "expression of said at least three maintenance genes" is to be "used" in the comparing step in the practice of the claimed method. Applicants have amended the claim to add the

phrase "as a control to normalize the expression of said gene in said plurality of samples" to describe how the expression of the maintenance genes is to be used. The expression of the experimental gene is measured in each sample in the plurality and the measurement of the expression of the gene from one sample is compared to the measurement of the expression of the gene in another sample after normalization of the measurements using the expression measurements of the maintenance genes. Applicant believes that this amendment obviates this rejection of the claims.

Claims 10-13 are considered allegedly indefinite over the recitation of the list of maintenance genes set forth in claim 13, since the list comprises mRNA and protein names, rather than gene names. Applicants have amended claim 13 to clarify that what is being measured is the expression of the gene encoding the proteins and mRNAs that are listed. It is readily apparent to a person skilled in the art that both protein and mRNA names may be used to define a gene. The claim does not specify whether protein or mRNA levels are being measured. Therefore, this rejection of Claims 10-13 is obviated.

The Examiner further alleges that the list of maintenance genes includes proteins having multiple subunits (e.g., ATP synthase), as well as some subunits included in those proteins, thereby allegedly making it unclear as to what molecules are encompassed by the claims. Applicants respectfully disagree. However, for the purpose of expediting the issuance of the claims, Applicants have removed "ATP synthase" from the list of maintenance genes in claim 13.

For the above reasons, the claim rejections under 35 U.S.C. § 112 should be withdrawn.

**C. Claim Rejections under 35 U.S.C. § 103(a)**

Claims 10-13 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over MacLeod *et al* in view of Kagawa *et al*. Applicants respectfully disagree.

The Examiner notes that Macleod *et al* do not disclose measuring at least three/five/ten of the maintenance genes recited in claim 13, but alleges that Kagawa *et al* teach "at least ten maintenance genes" that are encompassed by the instant claims as

written. Neither reference suggests the limitation(s) encompassed by the claims of the present invention. Moreover, the Examiner has not pointed out any suggestions or motivation to combine the two references and has thus failed to establish a *prima facie* case of obviousness.

Kagawa *et al* discuss ATP synthesis and disclose that although ATP synthase and oligomers supplying energy to  $F_0F_1$  are housekeeping, they are under a coordinated transcriptional control mechanism and their expression may be closely related to cell differentiation (see Abstract, paragraphs 4 and 6). Thus, Kagawa *et al*. teaches that they may not behave like typical housekeeping genes.


For the above reasons, the claim rejections under 35 U.S.C. § 103(a) should be withdrawn.

#### CONCLUSION

For the foregoing reasons, Applicants believe all the pending claims are now in condition for allowance and should be passed to issue. If the Examiner feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned at (408) 731-5000.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account 01-0431.

Respectfully submitted,

  
Sandra Wells  
Reg. No. 52,349

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Legal Department  
Affymetrix, Inc.  
3380 Central Expressway  
Santa Clara, CA 95051  
Tel: 408/731-5000  
Fax: 408/731-5392

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 APPLICANT: Pharmingen et al. DATE MAILED/RECEIVED: 8/26/03  
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